REMARKS

This Amendment is filed in response to the non-final Office Action dated July 8, 2008, and is respectfully submitted to be fully responsive to the rejections raised therein. Accordingly, favorable reconsideration on the merits and allowance are respectfully requested.

In the present Amendment, claim 1 has been amended to limit the method claim to treating human patients. Support for the amendment can be found in the specification on page 1, lines 19-27 and page 2, lines 9-11, for example. Furthermore, the recitation relating to the structural analogues of rapamycin has been deleted from the claim.

Claims 2 and 4 were directed to analogues of rapamycin and have therefore been canceled without prejudice.

Claim 3 has been amended to improve the claim format. Support for the amendment to claim 3 can be found in the specification on page 3 at lines 21-30, for example.

No new matter has been added. Entry of the Amendment is respectfully submitted to be proper. Upon entry of the Amendment, claims 1 and 3 will be all the claims pending in the application.

I. Response to Rejections Under 35 U.S.C. § 112, 1st and 2nd Paragraphs

Claims 3 and 4 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

Claims 1-4 are rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

Applicants traverse.

Claim 3 has been amended to provide antecedent basis for "modifier of a transcription process".

In addition, without acquiescing the merits of the rejection, the claims have been amended to delete the recitations of the analogues of rapamycin.

In view of the amendments to the claims, Applicants respectfully request that the rejections of claims 1 and 3 be withdrawn.

II. Response to Rejections Under 35 U.S.C. § 102(a) and § 103(a) based on Johnston

Claim 1 stands rejected under 35 U.S.C. § 102(a) as assertedly being anticipated by Johnston et al. Blood, 98(11): 410, 2001 ("Johnston").

Claims 1-4 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Johnston in view of Rachmilewitz, British Journal of Haematology, 91: 263-268, 1995 ("Rachmilewitz").

Applicants traverse the rejection.

Applicants respectfully submit that rapamycin is used to induce the expression of the gamma-globin gene in order to produce HbF. This utilization show a favorable clinical results in human patients suffering from beta-thalassemia. Particularly, in human beings, activation of the transcription of genes for gamma-globins in adult subjects leads to the production of foetal haemoglobin mimicking the phenotype HPFH (High Persistence of Foetal Haemoglobin) which confers a favorable clinical picture on patients suffering from beta-thalassaemia also in homozygotic form (4). (See, e.g., Specification at page 1, fourth paragraph).

Johnston discloses the use of rapamycin within the context of gene therapy, in order to induce the expression of erythropoietin (EPO) from an artificial construct based on AAV vectors containing the EPO gene and engineered transcription factors.

Applicants further submit that Johnston does not disclose rapamycin as an active agent. In fact, if, in the system of Johnston, rapamycin is administered in the absence of EPO expression (e.g. by withdrawing the transcription factors from the system), beta-thalassemia

will not be improved. This clearly indicates that rapamycin is not an active agent. In the system of Johnston, rapamycin is merely a transcription factor modulator, acting on the artificial construct based on the AAV vectors expressing inducible EPO.

The fact that the active agent in the treating system in Johnston is EPO and not rapamycin, is further demonstrated by the fact that when the beta-thalassemia mouse model is administered with AAV-CMVepo but without rapamycin, the anemia and abnormal red blood cell morphology is corrected. This is taught on lines 11-12 of Johnston.

This is not surprising, since the treatment system of Johnston is based on a gene therapy approach, in which the essential element is the expression of the foreign EPO gene.

It is also worth noting that according to lines 12-14 of Johnston, the expression of the EPO gene from the AAV-CMVepo construct is too high and unregulated, leading to severe polycythemia and death of the treated animals. The second, inducible construct was prepared and employed in order to overcome such drawbacks resulting from the expression of exceedingly high FPO levels.

However, polycythemia is unrelated to thalassemia. Polycythemia is a condition in which there is a net increase in the total number of red blood cells in the body. Quite to the contrary, thalassemia is a condition in which there is a genetic defect resulting in reduced rate of synthesis of one of the globin chains that make up hemoglobin.

Johnston teaches that in order to improve the condition of the beta thalassemic mice, one has to induce the expression of the EPO gene but at the same time, unregulated and too high expression of the EPO gene should be avoided, since this would lead to polycythemia which, in some respects, is the contrary of thalassemia.

Johnston does not teach nor suggest that rapamycin would be active as such in the treatment of beta thalassemia. At best, Johnston teaches that rapamycin could be considered as a means of preventing polycythemia, but surely not beta-thalassemia.

For at least the above reasons, the Johnston does not render the present claims anticipated or obvious.

Accordingly, withdrawal of the rejections is respectfully requested.

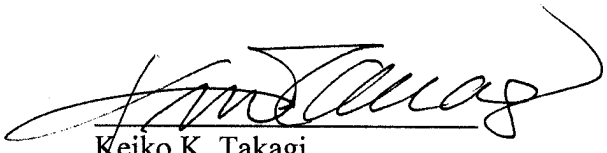
III. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited.

If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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